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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/235,875	01/22/1999	LARA MADISON	MBX020	2296

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EXAMINER	
KALLIS, RUSSELL	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 10/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/235,875	MADISON ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,7,10 and 14-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,7,10 and 14-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 6, 7, 10 and 14-21 are pending and examined.

Rejection of Claim 17 under 35 U.S.C. 112, second paragraph is withdrawn in view of Applicant's amendments.

Specification

The disclosure is objection to because of the following informalities: The previous objection, on page 21, line 25 of the specification, to the *A. caviae* PHB polymerase gene referenced in (Fukui & Doi, *J, Bacteriol.* 179: 4821-30 (1997)) as being incorrect also applies to the *A. caviae* PHB polymerase gene of Example 5 that also uses the plasmid pMBXc12J12 comprising the *A.* caviae PHA synthase gene as that on page 21, line 25, and throughout the specification the recitation of *A. caviae* PHB polymerase gene appears.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 1, 6, 7, 10 and 14-21 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection. This rejection is maintained for the reasons of record set forth in the Official action mailed 12/9/2002, 6/3/2003, 11/19/2003 and 5/05/2004. Applicant's arguments filed 8/05/2004 have been fully considered but they are not persuasive because Applicant has not responded to the NEW MATTER rejection.

The added claimed material which is not supported by the original disclosure is as follows: Newly amended Claim 1 recites "a phbC polymerase gene that encodes an enzyme that polymerizes 3-hydroxybutyryl CoA and 3-hydroxyhexanoyl-CoA". There is no support in the specification for a *phbC* polymerase gene encoding an enzyme that polymerizes hydroxybutyryl CoA and 3-hydroxyhexanoyl-CoA. The specification supports PHB polymerases from *Z. ramigera* that have a strict specificity for 3-hydroxy butyryl CoA and a PHB polymerase from *R. eutropha* that is highly specific for the 3-hydroxybutyryl CoA monomer and has shown a 7.5% activity towards 3-hydroxyvaleryl CoA, but there is no support in the specification for a *phbC* polymerase that polymerizes 3-hydroxybutyryl CoA and 3-hydroxyhexanoyl CoA. There is only speculation that the *phbC* gene from *N. salmonicolor* encodes a PHB polymerase that might have a wider substrate range than the other PHB biosynthetic enzymes on page 12 lines 1-6, but there is nothing that asserts that there is an isolated phbC gene encoding an enzyme that polymerizes 3-hydroxybutyryl CoA and 3-hydroxyhexanoyl-CoA. Applicant is invited to point to the page and line number in the specification where support can be found. Absent of such support, Applicant is required to cancel the new matter in the reply to this Office Action.

Claims 1, 6, 7, 10 and 14-21 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record set forth in the Official action mailed 12/9/2002, 6/3/2003, 11/19/2003 and 5/05/2004. Applicant's arguments filed 8/05/2004 have been fully considered but they are not persuasive.

Applicant asserts that support for Claim 1 can be found in Example 3 and Example 5 both of which disclose enzymes that can form a PHBH copolymer (response page 5). Applicant is arguing limitations that are not in the claims. Examples 3 and 5 are drawn to the PHA synthase gene (*phaC*) from *A. caviae* (see objection to the specification in previous office action and cited above) which is not a limitation found in any of the claims.

Applicant asserts that gene of the invention can be obtained from organisms that have been shown to incorporate3-hydroxyhexanoyl CoA (response page 5).The ability to isolate a gene does not adequately describe the gene nor does it demonstrate possession when considering that one would have to isolate that gene and then confirm that it has the claimed activity. Further, Applicant has not described a representative number of sequences encoding the various enzymes of the invention nor has there been a description of conserved regions that would define any of those broadly claimed categories of genes encoding the enzymes of the invention so that one would know that one was in possession of the claimed invention.

Applicant asserts that any of the publications listed on page 6 of the response taken from the Background of the Invention provide numerous sources of enzymes, including sequences that encode them (response pages 6-7). Only references authored by Steinbuchel and the U.S. Patents of Peoples and Sinskey listed on page 4 of the response collectively describe *phbCAB* genes from *A. eutrophus,* a PHA polymerase gene (*phaC*) from *Nocardia salmonicolur,* a *phaC* and *phbC* gene from *P. oleovorans*, and a *phbAB I* gene from *Zooglea ramigera*. This does not approach the "numerous examples" claimed in Applicant's response and combined with the teaches in the specification of genes encoding PHA synthase from *A. caviae* (*phaC*), and β-ketoacyl-CoA reductase (*phbB*) and β-ketothiolase (*phbA*) from *R. Eutropha* does not describe a

representative number of sequences that describe a genus of the broadly claimed phbA thiolase gene, phbB reductase gene, and especially the genus of a phbC polymerase gene encoding an enzyme that polymerizes 3-hydroxybutyryl CoA and 3-hydroxyhexanoyl CoA, of which none are described in this application.

Applicant asserts that they have sent results of GenBank searches for *acyl CoA synthase, acyl ACP thioesterase* and *ACP-CoA transacylase* sequences published before the January 22, 1998 priority date of the instant application (response page 7). The Examiner acknowledges Applicant's evidence for the claimed fatty acid biosynthetic genes prior to the effective filing date, however the rejection is maintained for the reasons set forth above.

Claims 1, 6, 7, 10 and 14-21 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of production of a polyhydroxyalkanoate containing 3-hydroxyhexanoate, by growing a bacterium transformed with a phaC gene from *A. caviae*, a phbA from *R. Eutropha* and a phbB gene from *R. Eutropha*; or by growing a bacterium transformed with a phaB gene from *R. Eutropha* and a phaJ gene from *A. caviae*, does not reasonably provide enablement for a method of production of a polyhydroxyalkanoate containing 3-hydroxyhexanoate, comprising providing a bacteria expressing a phbA thiolase gene, a phbB reductase gene, and a phbC polymerase gene encoding an enzyme that polymerizes 3-hydroxybutyryl CoA and 3-hydroxyhexanoyl CoA; further comprising a gene encoding a β-hydroxyacyl-ACP-coenzyme A transferase; or further comprising a phaJ gene encoding a D-specific enoyl-CoA hydratase; or further comprising the genes encoding the enzymes of Claim 17; or further comprising expressing genes encoding one or more fatty acid biosynthetic enzymes. The specification does not enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. This rejection is maintained for the reasons of record set forth in the Official action mailed 12/9/2002, 6/3/2003, 11/19/2003 and 5/05/2004. Applicant's arguments filed 8/05/2004 have been fully considered but they are not persuasive.

Applicant asserts that any of the publications listed on page 6 of the response taken from the Background of the Invention provide numerous sources of enzymes, including sequences that encode them (response pages 6-7). Only references authored by Steinbuchel and the U.S. Patents of Peoples and Sinskey listed on page 4 of the response collectively describe *phbCAB* genes from *A. eutrophus,* PHA polymerase gene (*phaC*) from *Nocardia salmonicolur, phaC* and *phbC* from *P. oleovorans*, and *phbAB* from *Zooglea ramigera*. This does not approach the "numerous examples" claimed in Applicant's response and combined with the teaches in the specification of genes encoding PHA synthase from *A. caviae* (*phaC*), and β-ketoacyl-CoA reductase (*phbB*) and β-ketothiolase (*phbA*) from *R. Eutropha* does not describe a representative number of sequences of a *phbA* thiolase gene, a *phbB* reductase gene, and a *phbC* polymerase gene encoding an enzyme that polymerizes 3-hydroxybutyryl CoA and 3-hydroxyhexanoyl CoA.

Applicant asserts that they have sent results of GenBank searches for *acyl CoA synthase, acyl ACP thioesterase* and *ACP-CoA transacylase* sequences published before the January 22, 1998 priority date of the instant application (response page 7). The Examiner acknowledges Applicant's evidence for the claimed fatty acid biosynthetic genes prior to the effective filing date, however the rejection is maintained for the reasons set forth above.

Applicant asserts that a representative number of genes encoding the enzymes of the invention were known in the art and identified in the specification as of the date of filing to

reasonably convey possession (response pages 8-10) and further asserts the fact that experimentation may be complex does not make it undue if it is typical in the art and that it is clear from the teachings in the specification that one of ordinary skill in the art could practice the invention without undue experimentation (response pages 10-11). Experimentation that is routine is not undue, however research typically involves complex and therefore unpredictable experimentation, and thus would require undue trial and error experimentation. The lack of a representative number of sequences that would enable a researcher to design PCR primers or a probe from conserved regions of a coding sequence required to practice the invention. For example, Applicant has not provided an example of a polynucleotide sequence encoding a phbC polymerase gene encoding an enzyme that polymerizes 3-hydroxybutyryl CoA and 3-hydroxyhexanoyl CoA. Isolation of this gene without sequence information to make primers for PCR or for designing a probe for probing a DNA library is an invitation to undue trial and error experimentation.

Applicant asserts that isolation and expression of the genes of the invention are routine and enzymes can easily be identified by their substrate specificity or their product formation i.e. polyhydroxybutyrate-co-polyhydroxyhexanoate (response page 12). Applicant's specification does not provide support for a phbC polymerase gene encoding an enzyme that polymerizes 3-hydroxybutyryl CoA and 3-hydroxyhexanoyl CoA. The specification only supports a *phbC* polymerase gene from *Nocardia salmonicolor* on page 12, lines 11-12. Further, See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a "mere germ of an idea does not constitute [an] enabling disclosure", and that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the

invention. Furthermore, See *In re Fisher,* 166 USPQ 18, 24(CCPA 1970) which teaches "That paragraph (35 USC 112, first) requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved."

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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October 7, 2004

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